**Effects of L-theanine-caffeine combination on sustained attention and inhibitory control among children with ADHD: a proof-of-concept neuroimaging RCT**

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We examined the acute effects of L-theanine, caffeine and their combination on sustained attention, inhibitory control and overall cognition in boys with attention deficit hyperactivity disorder (ADHD). L-Theanine (2.5 mg/kg), caffeine (2.0 mg/kg), their combination and a placebo were administered in a randomized four-way repeated-measures crossover with washout, to five boys (8-15 years) with ADHD. Functional magnetic resonance imaging (fMRI) was performed during a Go/NoGo task and a Stop-signal task ~ 1 h post-dose. NIH Cognition Toolbox was administered ~ 2 h post-dose. Treatment vs. placebo effects were examined in multi-level mixed-effects models. L-Theanine improved total cognition composite in NIH Cognition Toolbox (p = 0.040) vs. placebo. Caffeine worsened and L-theanine had a trend of worsening inhibitory control (i.e. increased Stop-signal reaction time; p = 0.031 and p = 0.053 respectively). L-Theanine-caffeine combination improved total cognition composite (p = 0.041), d-prime in the Go/NoGo task (p = 0.033) and showed a trend of improvement of inhibitory control (p = 0.080). L-Theanine-caffeine combination was associated with decreased task-related reactivity of a brain network associated with mind wandering (i.e. default mode network). L-Theanine-caffeine combination may be a potential therapeutic option for ADHD-associated impairments in sustained attention, inhibitory control and overall cognitive performance.

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